REMARKS

This Amendment is responsive to the Office Action mailed February 29, 2008. With this Amendment, claims 1-11 are amended, claim 12 is cancelled, and claims 13-14 are added. Applicants submit that claims 2-11, 13, and 14 are examinable along with the originally presented subject matter.

Support for the amendments to the claims can be found throughout the specification and claims as filed, including, e.g., original claims 2 and 5; page 3, line 20 through page 4, line 9; page 6, line 25 through page 7, line 7; page 7, lines 17-23; and the Examples described on pages 10-12.

Information Disclosure Statement

Applicants thank the Examiner for considering the Information Disclosure Statement filed on April 21, 2006, and for indicating such consideration by including an initialed and electronically signed copy of the Form PTO-1449 with the Office Action mailed February 29, 2008.

Applicants are submitting a Supplemental Information Disclosure Statement concurrently herewith and consideration of the information and documents cited therein is respectfully requested.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Office Action rejects claims 1, 6, 8, 9, and 10 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Office Action states that the specification fails to provide a representative number of species to adequately describe the genus of "any agent for controlling any action of a retinoid."

In response, Applicants submit that the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Furthermore, and while not acquiescing to the propriety of any of the assertions made in the rejection of the claims under 35 U.S.C. § 112, first paragraph (written description), Applicants respectfully submit that the amendment addresses the instant rejection and respectfully request withdrawal of the same.

In particular, Applicants submit that the specification fully describes the claimed subject matter including a medicament for prophylactic and/or therapeutic treatment of arteriosclerosis or a vascular disease due to intravascular physical injury, which comprises 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof as an active ingredient, and the recited methods of using 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof.

Applicants submit that the claimed subject matter was described in the specification in such a way as to convey to those skilled in the art that Applicants were in possession of the claimed invention at the time of filing. Applicants respectfully request

reconsideration and withdrawal of the written description rejection under 35 U.S.C. §112, first paragraph.

The Office Action also rejects claims 1, 6, 8, 9, and 10 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the Office Action states that "[t]he specification fails to provide any additional representative species of the claimed genus to show that applicant was in *possession* of the claimed genus of 'any agent for controlling any action of a retinoid'..." (emphasis added; see Office Action mailed February 29, 2008 at page 3, first full paragraph).

In response, Applicants submit that the specification provides sufficient guidance such that one of skill in the art could make and use the invention without undue experimentation. Furthermore, and while not acquiescing to the propriety of any of the assertions made in the rejection of the claims under 35 U.S.C. § 112 (enablement), Applicants respectfully submit that the amendment addresses the instant rejection and respectfully request withdrawal of the same.

In particular, Applicants submit that the specification provides sufficient guidance such that one of ordinary skill in the art would know how to make and use the claimed subject matter, including how to perform the claimed methods. Applicants further submit that the instantly disclosed invention, and in particular, the Examples found in the specification, show that the presently claimed subject matter has substantially no antiproliferative action on vascular endothelial cells, while at the same time having substantially antiproliferative action on vascular smooth muscle cells. As a result, the claimed subject matter exhibits effectiveness for the recited conditions. Furthermore,

Applicants submit that the Office is improperly applying a written description standard of *possession* in a rejection under *enablement*. In addition, the Office has not set forth any discussion of the *Wands* factors, or provided any rationale as to *why* the claimed subject matter does not meet the enablement requirement.

Applicants submit that the instant disclosure provides clear and sufficient guidance such that the claimed invention is enabled. Applicants respectfully request reconsideration and withdrawal of the rejections under the enablement requirement of 35 U.S.C. §112, first paragraph.

Claim Rejections – 35 U.S.C. § 102

The Office Action rejects claims 1-4, 6-8, and 12 under 35 U.S.C. § 102(b) as allegedly anticipated by Brown et al. (WO 00/10522; hereinafter BROWN).

The Office Action also rejects claim 1 under 35 U.S.C. § 102(b) as allegedly anticipated by Haxsen et al. (Circulation Research, 2001, Vol. 88, No. 6, pp. 637-644).

The Office Action also rejects Claims 9 and 10 under 35 U.S.C. § 102(b) as allegedly anticipated by Zhou et al. (Proc. Natl. Acad. Sci. USA, 1995, Vol. 92, pp. 7391-7395).

In response, Applicants submit that the claimed invention is not anticipated by the cited documents. In particular, Applicants submit that none of the cited documents disclose "[a] medicament for prophylactic and/or therapeutic treatment of arteriosclerosis or a vascular disease due to intravascular physical injury, which comprises 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof as an active ingredient." Neither do any of the documents disclose methods of treatment

comprising administering an effective amount of 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof to a mammal, as recited in the claims.

Applicants submit that the claimed subject matter is not anticipated by the cited documents and respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b).

Claim Rejections – 35 U.S.C. § 103

The Office Action rejects Claims 5 and 11 under 35 U.S.C. § 103(a) as allegedly unpatentable over BROWN in view of Kagechika et al. (Journal of Medicinal Chemistry, 1988, Vol. 31, No. 11, pp. 2182-2192; hereinafter KAGECHIKA). In particular, the Office Action states that BROWN teaches the use of retinoids and regulators of retinoid action for the prevention and/or treatment of vascular disease. The Office Action further states that BROWN does not teach 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof. For this missing feature, the Office relies upon KAGECHIKA. Finally, the Office Action states that "one of skill in the art would have been motivated to use Am80 as taught by Kagechika et al. having retinoic acid-like physiological activity as the retinoid in Brown et al." (see page 6, 3rd full paragraph of the Office Action mailed February 29, 2008).

In response, Applicants submit that the claimed subject matter is not disclosed or fairly suggested by BROWN in view of KAGECHIKA. The instantly disclosed invention, and in particular, the Examples found in the specification, show that the

presently claimed subject matter has substantially no antiproliferative action on vascular endothelial cells, while at the same time having substantially antiproliferative action on vascular smooth muscle cells. As a result, the claimed subject matter also exhibits effectiveness for the recited conditions.

More importantly, the pharmacological action of the claimed subject matter would not have been obvious to one of ordinary skill in the art, and the cited documents, either alone, or in combination, do not disclose or fairly suggest "[a] medicament for prophylactic and/or therapeutic treatment of arteriosclerosis or a vascular disease due to intravascular physical injury, which comprises 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof as an active ingredient." Neither do the cited documents, either alone or in combination, disclose or fairly suggest "[a] method of treating arteriosclerosis or a vascular disease due to intravascular physical injury comprising administering to a mammal an effective amount of a substance comprising 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof."

With regard to the Office's assertion that "one of skill in the art would have been motivated to use Am80 as taught by Kagechika et al. having retinoic acid-like physiological activity as the retinoid in Brown et al.," Applicants submit that the Office has not set forth any *reasons* or *rationale* as to why one of skill in the art would have combined the BROWN and KAGECHIKA teachings to treat arteriosclerosis and/or vascular disease due to intravascular physical injury. Applicants further submit that

simply stating that motivation exists is not sufficient; the Office must indicate *why* one of ordinary skill in the art would have combined the BROWN and KAGECHIKA teachings.

Applicants further submit that BROWN fails to disclose the recited methods of treatment for arteriosclerosis or vascular disease due to intravascular physical injury comprising administration of 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or a salt thereof as an active ingredient. The BROWN document also fails to disclose such methods for the suppression of granulation due to intravascular physical injury, the suppression of proliferation of neointima due to intravascular physical injury, the prophylactic and/or therapeutic treatment of hypercardia, and the suppression of fibrosis in hypercardia.

Applicants submit that the disclosed and claimed subject matter is not anticipated or fairly suggested and respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

The Office Action also rejects Claims 5 and 11 under 35 U.S.C. § 103(a) as allegedly unpatentable over BROWN in view of Murakami et al. (Clinical Cancer Research, 1999, Vol. 5, No. 9, pp. 2304-2310; hereinafter MURAKAMI).

In response, Applicants submit that the claimed invention is not anticipated or fairly suggested by the cited documents. In particular, Applicants submit that none of the cited documents disclose or suggest "[a] medicament for prophylactic and/or therapeutic treatment of arteriosclerosis or a vascular disease due to intravascular physical injury, which comprises 4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-